



# LSU School of Graduate Studies

## Neuroscience Center of Excellence

### *Dissertation Defense*

"Role of Homocysteine in the Pathophysiology of Alzheimer's Disease"

Javier Pacheco-Quinto

Recent epidemiological and clinical data suggest that elevated serum homocysteine levels may increase the risk of developing Alzheimer's disease (AD), but the underlying mechanisms are unknown. We tested the hypothesis that high homocysteine concentration may increase amyloid beta-peptide ( $A\beta$ ) levels in the brain and could therefore accelerate AD neuropathology. For this purpose, we developed a new *in vivo* model for studying the effect of hyperhomocysteinemia in brain amyloidosis. This model helped us to demonstrate for the first time an unequivocal correlation between  $A\beta$  and plasma homocysteine levels *in vivo*. We also found evidence that the increase in  $A\beta$  may be in part by dysregulation of a key enzyme for  $A\beta$  degradation, insulin degrading enzyme (IDE). Finally, we obtained data, which unexpectedly suggested the presence of a yet not identified  $A\beta$ -degrading enzyme that it is also inhibited by homocysteine.

**2:00pm Monday January 28, 2008**  
**8<sup>th</sup> Floor Neuroscience Center Conference Room**  
**LSU Lion's Building,**  
**2020 Gravier Street**